Physiologically Based Pharmacokinetic (PBPK) Modeling

Chemical Dosimetry
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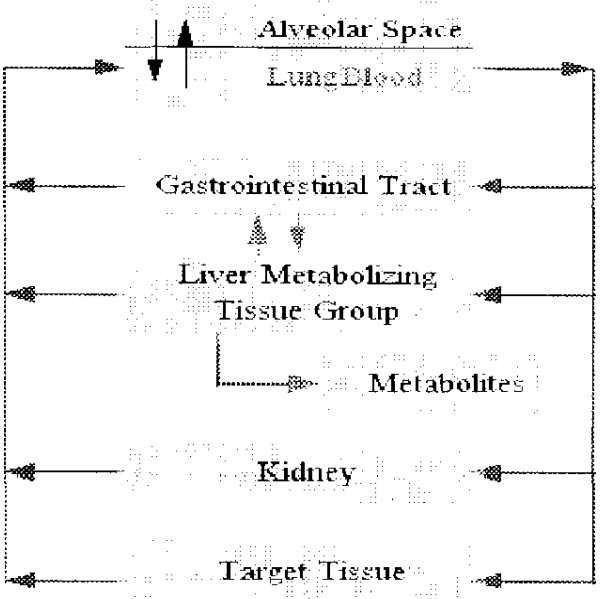
Physiologically based pharmacokinetic (PBPK) modeling is a powerful toxicological tool designed to convert an exposure (regardless of route) into a target tissue dose. A PBPK model is founded on known physiological processes (blood flow rates, tissues volumes, breathing rates, etc.), on chemical-specific processes (partition coefficients, chemical density, metabolic constants, molecular weight, etc.), and on species-dependent processes. Thus, a PBPK model can be developed and validated against the more readily available experimental animal data, and then extrapolated to predict concentrations of toxic compounds in human tissues following exposure. The complexity of the PBPK model is limited only by the quality of the scientific understanding of the processes involved. During the developmental stage, a PBPK model can help to identify data gaps and be used to focus future studies. Given enough sound scientific data, PBPK models can be used to extrapolate from a single acute to a chronic exposure, from a continuous to an intermittent exposure, from a high to a low exposure, and from a single chemical to a complex mixture exposure.



Perhaps the greatest impact in using a PBPK model to convert exposure into target tissue dose is the flexibility to perform these calculations on an individual basis. Models can be developed to individually track each person's unique physiological and/or metabolic characteristics. For example, a model could follow the change in blood flow and tissue size during pregnancy and at the same time predict the target tissue dose to a developing fetus. The metabolic rates in a model can be individually adjusted to account for enhanced (or decreased) metabolism of a particular compound when the person is on a specific pharmaceutical agent. A model can be adjusted to account for variations in the amount of body fat -- a potentially large reservoir for storing many organic compounds of toxicological significance.

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Source: https://www.industrydocuments.ucsf.edu/docs/qrdj0001

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Website maintained by Rob Stewart (trebor@pnl.gov).
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